IFW # AF/1654

Attorney Docket No. P66403US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: BAR et al.

Application No. 09/744,973 Art Unit: 1654

Filed: April 16, 2001 Examiner: A. Gupta

For: USE OF FIBROGEN MUTLIMERS

RESPONSE

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The instant paper responds to the final Office Action mailed November 19, 2003.

Claims 9-15 stand rejected under 35 USC 102(b) as being allegedly anticipated by *Brazilian J. Med. Biol. Res., 28*, 473-476, 1993 (Reis). Claims 9-15 stand rejected under 35 USC 103(a) as being allegedly unpatentable based on the combined teachings of WO 9422503 (Martinowitz) and Reis. Claims 9-15 stand rejected under 35 USC 103(a) as being allegedly unpatentable based on the combined teachings of WO 9833533 (Nur) and Reis. Reconsideration of the rejections under §102(b) and §103(a) is requested.

Reconsideration is requested for the same reasons set forth in applicants' amendment filed August 26, 2003, which arguments are incorporated herein by reference; and, further, as supported in the Declaration Under 37 CFR 1.132 of co-inventor Dr. Israel Nur (the "Nur declaration"), submitted concurrently herewith.

According to the statement of rejection, the arguments set forth in the previously filed amendment (incorporated herein by reference) are non-persuasive and, so, the rejections of record (set forth above) maintained because: "Applicants have not met their burden of proving the products [of the presently claimed invention] obtained are not the same [as the products obtained by Reis]" (final Office Action, page 4). The Rule 132 Declaration by Dr. Nur is submitted, herewith, as further *evidence* that the products obtained according to Reis are not, in fact, the same as the presently claimed products and, so, all limitations on the present claims are not met by Reis, taken alone, or in combination with Martinowitz or Nur, as alleged in the statements of rejection.

As alleged in the statement of rejection: "Applicants have not provided any evidence that the [prior art] decanting process yielded the removal [o]f multimers (Office Action, sentences bridging pages 3 and 4). According to the statement of rejection, applicants allegedly have the burden of providing such "evidence" in order to rebut the allegations of anticipation and obviousness set forth, therein.

The Rule 132 Declaration by Dr. Nur explains that, contrary to the allegations set forth in the statement of rejection, "Applicants *have* provided evidence that the prior art decanting process removes multimers (Nur declaration, paragraph 4). The Nur Declaration goes on to "discuss" the experiments and results reported in the subject application, which discussion is repeated, below, for the convenience of the examiner:

> Experimental samples were compared using electrophoreses on an agarose SDS gel. The samples were applied on the top of each lane in the electrophoretic field. Smaller protein molecules in the samples move faster than the larger protein molecules, thereby, separating the constituent proteins of each sample in accordance

> with their size/molecular weight. Details of the electrophoretic conditions are given in the paragraph bridging pages 4 and 5 of the subject application. After electrophoreses the proteins were blotted on an nitrocellulose membrane as described in the paragraph bridging pages 5 and 6 of the subject application. Results are shown in application figure 2; due to the immunodetection of fibrinogen, only fibrinogen monomers and fibrinogen multimers are visible in the figure.
>
> Lanes 4 to 11 (in figure 2) show results using different samples of the product of the present invention. Lane 2 shows a product commercially available as BERIPLAST from Aventis Pharma. BERIPLAST is prepared using "double cold precipitation" also described in Reis. Using "double cold precipitation," frozen plasma is thawed at 4 °C and centrifuged. The supernatant is removed and the cryoprecipitate is redissolved at 37 °C. The cryoprecipitate is then pooled, frozen, thawed, pooled again, and centrifuged. The resulting supernatant, which contains any fibrogen multimers, is decanted and discarded.

Accordingly, the *evidence* of record establishes that Reis fails to meet the presently claimed feature (limitation) "of a fibrin sealant comprising fibrinogen multimers having at least 6 fibrinogen units" produced by the recited method. In the words of the Nur declararion (¶5):

> As evidenced by the experiments (and results) reported in the subject application, as explained above, a product prepared by "double cold precipitation" is free of fibrinogen; whereas, the product prepared in accordance with the instant invention contains fibrinogen multimers.

Since Reis fails to meet at least one limitation on the present claims, anticipation under §102(b) based on Reis is negated. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). Accordingly, withdrawal of the §102(b) based on Reis appears to be in order.